REMARKS

Amendments to the Sequence Listing

Responsive to the "Notice to Comply with Requirements for Patent Applications Containing Nucleotide and/or Amino Acid Sequence Disclosures" dated October 29, 2002, Applicants have amended the Sequence Listing submitted on March 22, 2001 to correct the errors noted therein. In particular, the information contained in section <213> of the sequence listing has been corrected and SEQ ID NOs for all the sequences shown in Figures 2 and 3 have been provided.

In accordance with 37 C.F.R. §1.821(c) and (e), Applicants have submitted on even date herewith a computer readable form of the corrected sequence listing (diskette) which is identical in substance to the substitute pages 1-19 containing the corrected sequence listing submitted herewith. No new matter has been added to the application.

Amendments to the Specification and the Claims

The SEQ ID NOs within the specification and the pending claims have been amended to agree with the corrected sequence listing submitted on even date herewith. No new matter has been added to the application.

Attached hereto is a marked-up version of the changes made to the application by the current amendment. The attached page is captioned "Version with Markings to show changes made." Also attached hereto is a copy of all the pending claims as amended. This attached page is captioned "Pending Claims."

CONCLUSION

In view of the foregoing remarks, the application is in condition for allowance. If a telephone conversation with Applicants' Attorney would expedite the prosecution of the above-identified application, the Examiner is urged to call Applicants' Attorney at (617) 227-7400.

Respectfully submitted,
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Version with Markings to Show Changes Made

In the Specification:

The sequence listing has been replaced with a corrected sequence listing.

The paragraph found at page 3, lines 5-6, has been amended as follows:

Fig. 2 shows peptides of the invention of various lengths derived from *Lol p* V (SEQ ID NO: 3-29, 60).

The paragraph found at page 3, line 7, has been amended as follows:

Fig. 3 shows peptides of various lengths derived from Lol p I (SEQ ID NO:30-53, 55, 56, 61, 62).

The paragraph found at page 7, line 25 through page 8, line 6, has been amended as follows:

The present invention also provides nucleic acid sequences encoding peptides of the invention. Nucleic acid sequences used in any embodiment of this invention can be cDNAs encoding corresponding peptide sequences as shown in Fig. 2 (SEQ ID NO:3-29, 60). Such oligodeoxynucleotide sequences can be produced chemically or mechanically, using known techniques. A functional equivalent of an oligonucleotide sequence is one which is 1) a sequence capable of hybridizing to a complementary oligonucleotide to which the sequence (or corresponding sequence portions) of *Lol p* V as shown in Fig. 1 or fragments thereof hybridizes, or 2) the sequence (the corresponding sequence portions complementary to the nucleic acid sequences encoding the peptide sequence derived from *Lol p* V as shown in Fig. 2 and/or 3) a sequence which encodes a product (e.g., a polypeptide or peptide) having the same functional characteristics of the product encoded by the sequence (or corresponding sequence portion) of *Lol p* V as shown in Fig. 1. Whether a functional equivalent must meet one or more criteria will depend on its use (e.g., if it is to be used only as an oligoprobe, it need meet only the first or second criteria and if it is to be used to produce a *Lol p V* peptide of the invention, it need only meet the third criterion). The nucleic acid sequences of the invention also include RNA which can be transcribed from the DNA prepared as described above.

The paragraph found at page 20, lines 20-25, has been amended as follows:

Various isolated peptides of the invention derived from ryegrass pollen protein *Lol p* V are shown in Fig. 2 (SEQ ID NO:3-29, 60). Peptides comprising at least two regions, each region comprising at least one T cell epitope of *Lol p* V are also within the scope of the invention. As

used herein a region may include the amino acid sequence of a peptide of the invention as shown in Fig. 2 or the amino acid sequence of a portion of such peptide.

The paragraph found at page 24, line 20 through page 25, line 16, has been amended as follows:

Peptides derived from the *Lol p* V protein allergen which can be used for therapeutic purposes comprise at least one T cell epitope of *Lol p* V and comprise all or a portion of the following peptides: LPIX-1 (SEQ ID NO:3), LPIX-1.1 (SEQ ID NO:~~3~~ 59), LPIX-2 (SEQ ID NO:4), LPIX-2.1 (SEQ ID NO:4 60), LPIX-3 (SEQ ID NO:5), LPIX-4 (SEQ ID NO:6), LPIX-5 (SEQ ID NO:7), LPIX-6 (SEQ ID NO:8), LPIX-7 (SEQ ID NO:9), LPIX-8 (SEQ ID NO:10), LPIX-9 (SEQ ID NO:11), LPIX-10 (SEQ ID NO:12), LPIX-11 (SEQ ID NO:13), LPIX-12 (SEQ ID NO:14), LPIX-13 (SEQ ID NO:15), LPIX-14 (SEQ ID NO:16), LPIX-15 (SEQ ID NO:17), LPIX-16 (SEQ ID NO:18), LPIX-17 (SEQ ID NO:19), LPIX-18 (SEQ ID NO:20), LPIX-19 (SEQ ID NO:21), LPIX-20 (SEQ ID NO:22), LPIX-21 (SEQ ID NO:23), LPIX-22 (SEQ ID NO:24), LPIX-23 (SEQ ID NO:25), LPIX-24 (SEQ ID NO:26), LPIX-26 (SEQ ID NO:28), and LPIX-27 (SEQ ID NO:29) (the sequences of which are shown in Fig. 2) wherein the portion of the peptide preferably has a mean T cell stimulation index (S.I.) equivalent to, or greater than the mean T cell stimulation index of the peptide from which it is derived (e.g. as shown in Fig. 5, the S.I. for LPIX-16 (SEQ ID NO:18) is shown above the bar to be 3.7, therefore any portion of LPIX-16 preferably has a mean S.I. of 3.7). Even more preferably peptides derived from the *Lol p* V protein allergen which can be used for therapeutic purposes comprise all or a portion of the following peptides: LPIX-4 (SEQ ID NO:6), LPIX-5 (SEQ ID NO:7), LPIX-6 (SEQ ID NO:8), LPIX-8 (SEQ ID NO:10), LPIX-9 (SEQ ID NO:11), LPIX-11 (SEQ ID NO:13), LPIX-12 (SEQ ID NO:14), LPIX-16 (SEQ ID NO:18), LPIX-17 (SEQ ID NO:19), LPIX-19 (SEQ ID NO:21), LPIX-20 (SEQ ID NO:22), LPIX-23 (SEQ ID NO:25), and LPIX-26 (SEQ ID NO:28) as shown in Fig. 2. Even more preferably, peptides derived from Lol p V protein allergen which can be used for therapeutic purposes comprise all or a portion of the following peptides: LPIX-1 (SEQ ID NO:3), LPIX-2 (SEQ ID NO:4), LPIX-3 (SEQ ID NO:5), LPIX-4 (SEQ ID NO:6), LPIX-5 (SEQ ID NO:7), LPIX-6 (SEQ ID NO:8), LPIX-7 (SEQ ID NO:9), LPIX-8 (SEQ ID NO:10), LPIX-9 (SEQ ID NO:11), LPIX-10 (SEQ ID NO:12), LPIX-11 (SEQ ID NO:13), LPIX-12 (SEQ ID NO:14), LPIX-13 (SEQ ID NO:15), LPIX-14 (SEQ ID NO:16), LPIX-15 (SEQ ID NO:17), LPIX-16 (SEQ ID NO:18), LPIX-17 (SEQ ID NO:19), LPIX-18 (SEQ ID NO:20), LPIX-19 (SEQ ID NO:21), LPIX-20 (SEQ ID NO:22), LPIX-21 (SEQ ID NO:23), LPIX-22 (SEQ ID NO:24), LPIX-23 (SEQ ID NO:25), LPIX-24 (SEQ ID NO:26), LPIX-26 (SEQ ID NO:28), and LPIX-27 (SEQ ID NO:29).

The paragraph found at page 25, line 17 through page 26, line 4, has been amended as follows:

One embodiment of the present invention features a peptide or portion thereof of *Lol p* I which comprises at least one T cell epitope of the protein allergen and has a formula X_n-Y-Z_m. According to the formula, Y is an amino acid sequence selected from the group consisting of LPIX-1 (SEQ ID NO: 3), LPIX-1.1 (SEQ ID NO: ~~3~~ 59), LPIX-2 (SEQ ID NO: 4), LPIX-2.1 (SEQ ID NO:4 60), LPIX-3 (SEQ ID NO: 5), LPIX-4 (SEQ ID NO: 6), LPIX-5 (SEQ ID NO: 7), LPIX-6 (SEQ ID NO: 8), LPIX-7 (SEQ ID NO: 9), LPIX-8 (SEQ ID NO: 10), LPIX-9 (SEQ ID NO: 11), LPIX-10 (SEQ ID NO: 12), LPIX-11 (SEQ ID NO: 13), LPIX-12 (SEQ ID NO: 14), LPIX-13 (SEQ ID NO: 15), LPIX-14 (SEQ ID NO: 16), LPIX-15 (SEQ ID NO: 17), LPIX-16 (SEQ ID NO: 18), LPIX-17 (SEQ ID NO: 19), LPIX-18 (SEQ ID NO: 20), LPIX-19 (SEQ ID NO: 21), LPIX-20 (SEQ ID NO: 22), LPIX-21 (SEQ ID NO: 23), LPIX-22 (SEQ ID NO: 24), LPIX-23 (SEQ ID NO: 25), LPIX-24 (SEQ ID NO: 26), LPIX-26 (SEQ ID NO: 28), and LPIX-27 (SEQ ID NO: 29) (the sequences of which are shown in Fig. 2). In addition, X_n are amino acid residues contiguous to the amino terminus of Y in the amino acid sequence of the protein allergen and Z_m are amino acid residues contiguous to the carboxy terminus of Y in the amino acid sequence of the protein allergen. In the formula, n is 0-30 and m is 0-30. Preferably, the peptide or portion thereof has a mean T cell stimulation index equivalent to greater than the mean T cell stimulation index of Y as shown in Fig. 4. Preferably, amino acids comprising the amino terminus of X and the carboxy terminus of Z are selected from charged amino acids, i.e., arginine (R), lysine (K), histidine (H), glutamic acid (E) or aspartic acid (D); amino acids with reactive side chains, e.g., cysteine (C), asparagine (N) or glutamine (Q); or amino acids with sterically small side chains, e.g., alanine (A) or glycine (G). Preferably n and m are 0-5; most preferably n + m is less than 10.

In the Claims

Claims 1, 29, and 42 have been amended as follows:

1. (Amended) An isolated peptide of *Lol p* V wherein said peptide comprises at least one T cell epitope of *Lol p* V, said peptide having at least 7, but no more than 100, amino acid residues comprising an amino acid sequence selected from the group consisting of amino acid sequences as shown in Fig. 2 of peptides LPIX-1 (SEQ ID NO:3), LPIX-1.1 (SEQ ID NO:~~3~~ 59), LPIX-2 (SEQ ID NO:4), LPIX-2.1 (SEQ ID NO: 4 60), LPIX-3 (SEQ ID NO:5), LPIX-4 (SEQ ID NO:6) LPIX-5 (SEQ ID NO:7), LPIX-6 (SEQ ID NO:8), LPIX-7 (SEQ ID NO:9), LPIX-8 (SEQ ID NO:10), LPIX-9 (SEQ ID NO:11), LPIX-10 (SEQ ID NO:12), LPIX-11 (SEQ ID NO:13), LPIX-12 (SEQ ID NO:14), LPIX-13 (SEQ ID NO:15), LPIX-14 (SEQ ID NO:16),

LPIX-15 (SEQ ID NO:17), LPIX-16 (SEQ ID NO:18), LPIX-17 (SEQ ID NO:19), LPIX-18 (SEQ ID NO:20), LPIX-19 (SEQ ID NO:21), LPIX-20 (SEQ ID NO:22), LPIX-21 (SEQ ID NO:23), LPIX-22 (SEQ ID NO:24), LPIX-23 (SEQ ID NO:25), LPIX-24 (SEQ ID NO:26), LPIX-26 (SEQ ID NO:28), and LPIX-27 (SEQ ID NO:29).

29. (Amended) A composition comprising a pharmaceutically acceptable carrier or diluent and at least two peptides, each peptide comprising at least one T cell epitope, wherein at least one peptide comprises an amino acid sequence or portion thereof derived from *Lol p* V which is selected from the group consisting of: LPIX-1 (SEQ ID NO:3), LPIX-1.1 (SEQ ID NO:~~3~~ 59), LPIX-2 (SEQ ID NO:4), LPIX-2.1 (SEQ ID NO: 4 60), LPIX-3 (SEQ ID NO:5), LPIX-4 (SEQ ID NO:6) LPIX-5 (SEQ ID NO:7), LPIX-6 (SEQ ID NO:8), LPIX-7 (SEQ ID NO:9), LPIX-8 (SEQ ID NO:10), LPIX-9 (SEQ ID NO:11), LPIX-10 (SEQ ID NO:12), LPIX-11 (SEQ ID NO:13), LPIX-12 (SEQ ID NO:14), LPIX-13 (SEQ ID NO:15), LPIX-14 (SEQ ID NO:16), LPIX-15 (SEQ ID NO:17), LPIX-16 (SEQ ID NO:18), LPIX-17 (SEQ ID NO:19), LPIX-18 (SEQ ID NO:20), LPIX-19 (SEQ ID NO:21), LPIX-20 (SEQ ID NO:22), LPIX-21 (SEQ ID NO:23), LPIX-22 (SEQ ID NO:24), LPIX-23 (SEQ ID NO:25), LPIX-24 (SEQ ID NO:26), LPIX-26 (SEQ ID NO:28), and LPIX-27 (SEQ ID NO:29) (as shown in Fig. 2), and wherein at least one peptide comprises an amino acid sequence or portion thereof derived from *Lol p* I which is selected from the group consisting of: LPI-1 (SEQ ID NO:30), LPI-1.1 (SEQ ID NO:31), LPI-2 (SEQ ID NO:32), LPI-3 (SEQ ID NO:55), LPI-4 (SEQ ID NO:33), LPI-4.1 (SEQ. ID NO:34), LPI-5 (SEQ ID NO:35), LPI-6 (SEQ ID NO:36), LPI-7 (SEQ ID NO:37), LPI-8 (SEQ ID NO:38), LPI-9 (SEQ ID NO:39), LPI-10 (SEQ ID NO:40), LPI-11 (SEQ ID NO:41), LPI-12 (SEQ ID NO:42), LPI-13 (SEQ ID NO:43), LPI-14 (SEQ ID NO:44), LPI-15 (SEQ ID NO:45), LPI-16 (SEQ ID NO:46), LPI-16.1(SEQ ID NO:47), LPI-17 (SEQ ID NO:48), LPI-18 (SEQ ID NO:49), LPI-19 (SEQ ID NO:50), LPI-20 (SEQ ID NO:56), LPI-21 (SEQ ID NO:51), LPI-22 (SEQ ID NO:52), and LPI-23 (SEQ ID NO:53) (as shown in Fig. 3).

42. (Amended) All or a portion of an isolated peptide of *Lol p I*, said peptide or portion thereof comprising at least one T cell epitope of said protein allergen, said peptide having the formula X_n-Y-Z_m, wherein Y is an amino acid sequence selected from the group consisting of: LPIX-1 (SEQ ID NO:3), LPIX-1.1 (SEQ ID NO:~~3~~ 59), LPIX-2 (SEQ ID NO:4), LPIX-2.1 (SEQ ID NO: 4 60), LPIX-3 (SEQ ID NO:5), LPIX-4 (SEQ ID NO:6) LPIX-5 (SEQ ID NO:7), LPIX-6 (SEQ ID NO:8), LPIX-7 (SEQ ID NO:9), LPIX-8 (SEQ ID NO:10), LPIX-9 (SEQ ID NO:11), LPIX-10 (SEQ ID NO:12), LPIX-11 (SEQ ID NO:13), LPIX-12 (SEQ ID NO:14), LPIX-13 (SEQ ID NO:15), LPIX-14 (SEQ ID NO:16),

LPIX-15 (SEQ ID NO:17), LPIX-16 (SEQ ID NO:18), LPIX-17 (SEQ ID NO:19), LPIX-18 (SEQ ID NO:20), LPIX-19 (SEQ ID NO:21), LPIX-20 (SEQ ID NO:22), LPIX-21 (SEQ ID NO:23), LPIX-22 (SEQ ID NO:24), LPIX-23 (SEQ ID NO:25), LPIX-24 (SEQ ID NO:26), LPIX-26 (SEQ ID NO:28), and LPIX-27 (SEQ ID NO:29) wherein X_n are amino acid residues contiguous to the amino terminus of Y in the amino acid sequence of said protein allergen, wherein Z_m are amino acid residues contiguous to the carboxy terminus of Y in the amino acid sequence of said protein allergen, wherein n is 0-30 and wherein m is 0-30.

Application No.: 08/737904

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

☒ 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to these regulations, published at 1114 OG 29, May 15, 1990 and at 55 FR 18230, May 1, 1990.

☐ 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).

☐ 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).

☐ 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."

☐ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).

☐ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable from of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).

☒ 7. Other: See enclosed Not

Applicant Must Provide:

☒ An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".

☒ An initial or substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.

☒ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (703) 308-4216
For CRF Submission Help, call (703) 308-4212
For PatentIn software help, call (703) 308-6856

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